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Catalytic Antibodies

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Document Version

Publisher's PDF, also known as Version of record

Publication date:

2005

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):

Janssen, D. B. (2005). Catalytic Antibodies.

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The Facts of Biological Reactions

Catalytic Antibodies

Edited by Ehud Keinan.

Wiley-VCH, Weinheim 2004. xxx + 586 pp.,
hardcover € 159.00.—ISBN 3-527-30688-9

Almost two decades ago, the seminal papers of R. A. Lerner, P. G. Schulz and their co-workers in *Science* showed that antibodies that were raised against transition-state analogues could catalyze chemical reactions. This description of catalytic antibodies provided experimental proof for L. Pauling's original proposal in 1940 that transition-state binding was a key feature of enzyme catalysis, and also confirmed the prediction of W. P. Jencks, who wrote in 1969 that an antibody against a transition-state mimic should be able to act as a catalyst. Since 1986, the field of catalytic antibodies has become one of the most fascinating areas in biomolecular science, with numerous beautiful contributions. Structural studies on various classes of catalytic antibodies and analysis of different generations of catalytic antibodies have revealed detailed insights in their molecular mechanisms and in the way they evolve. Catalytic antibodies have been made that catalyze unusual reactions, including bimolecular Diels–Alder additions and intramolecular rearrangements with chemically unfavourable selectivity. But the implications go further. For example, conversions of biotechnological relevance are emerging with the development of antibodies that catalyze stereoselective transacylations and aldol condensations. Indeed, catalytic antibodies have found applications in small-scale synthesis of natural products, and



biomedical applications are also being developed.

The book edited by E. Keinan provides an excellent overview of the state of the art in the field. It describes different categories of catalytic antibodies, their reaction mechanisms and catalytic properties, as well as structural aspects. It also presents various reaction types, application areas and practical aspects related to antibody production, screening and purification. The book is particularly attractive because the description of experimental results is generally put into a broader functional and mechanistic context. This approach has delivered a book that is a pleasure to read, not only for those who are quickly seeking specific and detailed information about antibody catalysis, but also for readers with a more general interest in biological catalysis and enzymology.

For an enzymologist, one of the striking observations about catalytic antibodies is that they generally have a much lower catalytic activity than enzymes. Even though antibodies can catalyze reactions for which there is no enzymatic equivalent available, this low catalytic rate has certainly hindered their penetration into industrial biocatalysis, where k_{cat} values usually are more important than the $k_{\text{cat}}/k_{\text{uncat}}$ value that is often used to describe the catalytic power of an antibody. The book discusses some of the fundamental causes of this difference in catalytic power, and, in this way, also points to gaps in our understanding of enzyme catalysis. Coordinated motions along the reaction coordinate involving enzyme and substrate are still difficult to describe, but might turn out to be of key importance for the difference in catalytic activity between enzymes and abzymes. Evidently, this type of functionality will not easily evolve into a catalytic antibody during selection for binding of a transition state analogue, al-

though directed evolution and reactive immunization might help to approach solutions. This is just an example of the more general type of thinking that the book evokes.

The book is composed of 19 chapters that are contributed by top experts in the field. It is an advanced text in the sense that basic biochemistry and protein chemistry are not included, in view of the topic, this is fully justified. On some topics, there is significant duplication between different chapters. For example, the antibodies that catalyze ferrocyclase-, chorismate mutase-, and the oxy-Cope rearrangement reactions are discussed twice or even three times in different chapters. This can be difficult to prevent if a certain level of completeness for each chapter has to be achieved, and is certainly not disturbing. Overall, the book is technically very well prepared. The text is lucid and precise, and illustrations are clear and remarkably consistent in lay-out and quality for a multiauthored volume. There are very few errors in graphs and references, mostly typographical and again not disturbing. This is certainly a book that is not made superfluous by on-line access to research journals and reviews. The book's front cover is beautifully illustrated and its symbolism will evoke a moment of thought about the place of books and science in the cultural history of mankind.

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DOI: 10.1002/cbic.200500126